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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/926,002	10/30/2001	Ulf Schroder	SCHR300/ REF	6626

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EXAMINER
FORD, VANESSA L

ART UNIT	PAPER NUMBER
1645	12

DATE MAILED: 06/03/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/926,002	SCHRODER ET AL.	
	Examiner	Art Unit	
	Vanessa L. Ford	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 December 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *11-46* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11-46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☒ Interview Summary (PTO-413) Paper No(s). *11* .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. This Office Action is responsive to Applicant's response filed 13 December 2002.

Rejections Withdrawn

2. In view of Applicant's amendment and response the following rejections have been withdrawn:

a) The rejection of claims 11-15 under 35 U.S.C. 103(a), pages 3-5, paragraph 5 of the previous Office action.

b) The rejection of claims 11-16, 18-27 and 29-36 under 35 U.S.C. 103(a), pages 5-7, paragraph 6 of the previous Office action.

c) The rejection of claims 11-15, 20-24 and 29-33 under 35 U.S.C. 103(a), pages 7-9 paragraph 7 of the previous Office action.

d) The rejection of claims 11-16, 18-27 and 29-36 under 35 U.S.C. 103(a), pages 9-11, paragraph 8 of the previous Office action.

e) The rejection of claims 11-37 under 35 U.S.C. 103(a), page 11, paragraph 9 of the previous Office action.

f) The rejection of claims 38-42 under 35 U.S.C. 103(a), pages 12-14, paragraph 10 of the previous Office action.

g) The rejection of claims 38-45 under 35 U.S.C. 103(a), pages 14-15, paragraph 11 of the previous Office action.

h) The rejection of claims 38-45 under 35 U.S.C. 103(a), pages 15-16, paragraph 12 of the previous Office action.

New Grounds of Rejection

Claim Objections

3. Claims 13-14, 16, 22-23, 31-32 and 40 are objected to for the following informalities:

Claim 13 recites "toroid" should be "toxoid".

Claim 14 recites "toroid" should be "toxoid".

Claim 14 recites "derived form" should be "derived from".

Claim 16 recites "toroid" should be "toxoid".

Claim 22 recites "toxid" should be "toxoid".

Claim 23 recites "toroid" should be "toxoid".

Claim 31 recites "toroid" should be "toxoid".

Claim 32 recites "toroid" should be "toxoid".

Claim 40 recites "toxid" should be "toxoid".

Correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 11, 13, 14, 20, 22, 29, 31, 32, 38 and 40 recite the term "derived from". It is unclear as to what the applicant is referring? Thus, the metes and bounds of "derived from" cannot be ascertained. Clarification as to the meaning of this term is required.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claims 11-36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schroder *(WO 97/47320, published December 1997)* in view of *Svenson (WO 97/35613, published October 1997)* and in further view of Hamasur et al *(Vaccine, 17, 1999, 2853-2861).*

Claims 11-36 are drawn to a vaccine formulation comprising as adjuvant one or more substances selected from a) monoglyceride preparations having 80% monoglyceride content, b) fatty acids and c) an immunizing component consisting of active carbohydrate moieties (ACM) derived from *Mycobacterium tuberculosis* which are each covalently coupled, possibly via identical divalent bride groups to immunogenically active carrier (IAC).

Schroder teaches a pharmaceutical formulation and vaccines for parenteral or mucosal administration of antigens and/or vaccines to humans and animals comprising monoglyceride preparations having at least 80% monoglyceride content and where the acyl group contains from 6 to 24 carbon atoms together with fatty acids where the number of carbon atoms may be varied between 4 and 22 (see the Abstract and Examples 4 and 6). Schroder teaches that the monoglycerides of the invention may have a purity of more than 80% preferably more than 90%, more preferably over 95% is used (pages 4-5). Schroder teaches that the vaccine composition may contain additional pharmaceutical excipients and the formation may comprise any antigen and/or vaccine selected among all the antigen and/or vaccines relevant to humans and animals (page 5).

Schroder does not teach the use of antigenically active carbohydrate moieties (ACM) (pages 9-10).

Svenson teaches a vaccine comprising antigenically active carbohydrate moieties (ACM) (pages 9-10). Svenson teaches that the antigenically active carbohydrate moieties (ACM) of the immunogenic products derived from bacterial O-polysaccharides and/or capsular polysaccharides (pages 3). Svenson teaches that the immunologically active carriers (IAC) of the immunogenic product of the invention is preferably derived from polypeptides and in a preferred embodiment of the invention said polypeptides is tetanus toxoid, diphtheria toxoid, cholera subunit B or Protein D from *H. influenzae* (page 4).

Schroder and Svenson as combined *supra* do not teach lipoarabinomannan-tetanus toxoid (LAM-TT).

Hamasur et al teach a lipoarabinomannan (LAM) preparations derived from *Mycobacterium tuberculosis* strain H37 Rv covalently conjugated to tetanus toxoid and a cross reactive mutant (CRM197) diphtheria toxoid (see the Abstract) (page 2857, 1st column and Table 2, page 2859). Hamasur et al teach that the both types of LAM oligosaccharide protein conjugates proved to be highly immunogenic, inducing a boosterable T helper cell dependent IgG response and these conjugates are currently being evaluated as components in subcellular experimental TB vaccine (see the Abstract). Claim limitations such as packaging the vaccine as an aerosol, spray or nose-drop package is being viewed as a limitation of design choice.

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was to add the active carbohydrate moieties (ACM) of Svenson to the vaccine formulation comprising a monoglyceride preparation as taught by Schroder because Schroder teaches that a combination between a monoglyceride and a fatty acid can stimulate the immune system to produce antibodies and induce protective immunity (page 7, lines 6-9) and it would be obvious to add the lipoarabinomannan (LAM) derived from *Mycobacterium tuberculosis* conjugated to tetanus toxoid as taught by Hamasur to the vaccine formulation of Schroder because Schroder teaches that the formation may comprise any antigen and/or vaccine selected among all the antigen and/or vaccines relevant to humans and animals (page 5). It would have been expected barring evidence to the contrary, that a vaccine formulation comprising LAM

conjugated to tetanus toxoid, monoglycerides and active carbohydrate moieties (ACM) would provided an excellent vaccine formulation against *Mycobacterium tuberculosis* because Hamasur et al teach that LAM derived from *Mycobacterium tuberculosis* conjugated to tetanus toxoid have been to be highly immunogenic, inducing a boosterable T helper cell dependent IgG response (see the Abstract), have indicated that they contain important antigenic epitopes, and these conjugates are currently being evaluated as components in subcellular experimental TB vaccine (page 2860) and Schroder teaches that a combination between a monoglyceride and a fatty acid (an adjuvant composition) can stimulate the immune system to produce antibodies and induce protective immunity (page 7, lines 6-9).

6. Claims 11-37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schroder in view of Svenson in view of Hamasur et al as applied to claims 11-36 above and further in Van Nest et al *(U. S. Patent No. 6,451,325, published September 17, 2992).*

Claims 11-37 are drawn to vaccine formulation comprising as adjuvant one or more substances selected from a) monoglyceride preparations having 80% monoglyceride content, b) fatty acids and c) an immunizing component consisting of active carbohydrate moieties (ACM) derived from *Mycobacterium tuberculosis* which are each covalently coupled, possibly via identical divalent bride groups to immunogenically active carrier (IAC) and further comprising soybean oil.

The teachings of Schroder, Svenson and Hamasur et al have been discussed above.

Van Nest et al teach the use of any metabolizable oil (for example, soybean oil) in an adjuvant formulation (column 3, lines 62-67 – column 4, lines 1-11). Van Nest et al teach that the oil component of the adjuvant can be present in an amount from 0.5% to 20% by volume (column 4, lines 49-53).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention to add soybean oil as taught by Van Nest et al to the vaccine formulation as combined above because Schroder teaches that the vaccine composition may contain additional pharmaceutical excipients may be added to the vaccine formation (page 5) and Van Nest et al teach that metabolizable oils such as soybean oil are used in vaccines because unmetabolizable oils when administered may cause abscesses, granulomas or even carcinomas and meat of birds and animals vaccinated with oil other than metabolizable oils may be unacceptable for human consumption due to the deleterious effect that unmetabolizable oils have on the consumer (column 3, lines 62-67 and column 4, lines 1-3).

7. Claims 38-45 are rejected under 35 U.S.C. 103(a) as being unpatentable over *(WO 97/47320, published December 1997)* in view of *Svenson, WO 97/35613, published October 1997)* and in further view of Hamasur et al *(Vaccine, 17, 1999, 2853-2861).*

Claims 38-45 are drawn to a method of vaccinating a mammal against mycobacterium having antigenically active carbohydrate moieties (ACM) derived from *Mycobacterium tuberculosis* which comprises mucosal administration to the mammal of a protection-inducing amount of a tuberculosis vaccine formulation comprising as adjuvant one or more substances.

Schroder teaches a method of vaccinating animals using a pharmaceutical formulation for parenteral or mucosal administration of antigens and/or vaccines to humans and animals comprising monoglyceride preparations having at least 80% monoglyceride content and where the acyl group contains from 6 to 24 carbon atoms together with fatty acids where the number of carbon atoms may be varied between 4 and 22 (see the Abstract and Examples 4 and 6). Schroder teaches that the monoglycerides of the invention may have a purity of more than 80% preferably more than 90%, more preferably over 95% is used (pages 4-5). Schroder teaches that the vaccine composition may contain additional pharmaceutical excipients and the formation may comprise any antigen and/or vaccine selected among all the antigen and/or vaccines relevant to humans and animals (page 5).

Schroder does not teach the use of antigenically active carbohydrate moieties (ACM) (pages 9-10).

Svenson teaches a method of vaccinating animals with antigenically active carbohydrate moieties (ACM) (pages 9-10). Svenson teaches that the antigenically active carbohydrate moieties (ACM) of the immunogenic products derived from bacterial O-polysaccharides and/or capsular polysaccharides (pages 3). Svenson teaches that

the immunologically active carriers (IAC) of the immunogenic product of the invention is preferably derived from polypeptides and in a preferred embodiment of the invention said polypeptides is tetanus toxoid, diphtheria toxoid, cholera subunit B or Protein D from *H. influenzae* (page 4).

Schroder and Svenson as combined *supra* do not teach lipoarabinomannan-tetanus toxoid (LAM-TT).

Hamasur et al teach a method of immunizing animals with lipoarabinomannan (LAM) derived from *Mycobacterium tuberculosis* strain H37 Rv covalently conjugated to tetanus toxoid and a cross reactive mutant (CRM197) diphtheria toxoid (see the Abstract) (page 2857, 1st column and Table 2, page 2859). Hamasur et al teach that the both types of LAM oligosaccharide protein conjugates proved to be highly immunogenic, inducing a boosterable T helper cell dependent IgG response and these conjugates are currently being evaluated as components in subcellular experimental TB vaccine (see the Abstract).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was to add the active carbohydrate moieties (ACM) of Svenson to the vaccine formulation comprising a monoglyceride preparation used in the method of vaccinating animals by mucosal administration as taught by Schroder because Schroder teaches that a combination between a monoglyceride and a fatty acid can stimulate the immune system to produce antibodies and induce protective immunity (page 7, lines 6-9) and it would be obvious to add the lipoarabinomannan (LAM) derived from *Mycobacterium tuberculosis* conjugated to tetanus toxoid as taught by

Hamasur to the vaccine formulation of Schroder because Schroder teach that the formation may comprise any antigen and/or vaccine selected among all the antigen and/or vaccines relevant to humans and animals (page 5). It would have been expected barring evidence to the contrary, that a vaccine formulation comprising LAM conjugated to tetanus toxoid, monoglycerides and active carbohydrate moieties (ACM) would be an effective vaccine formulation used in the method of vaccinating animals against *Mycobacterium tuberculosis* because Hamasur et al teach that LAM derived from *Mycobacterium tuberculosis* conjugated to tetanus toxoid have been to be highly immunogenic, inducing a boosterable T helper cell dependent IgG response (see the Abstract), have indicated that they contain important antigenic epitopes, and these conjugates are currently being evaluated as components in subcellular experimental TB vaccine (page 2860) and Schroder teach that a combination between a monoglyceride and a fatty acid (an adjuvant composition) can stimulate the immune system to produce antibodies and induce protective immunity (page 7, lines 6-9).

8. Claims 38-46 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schroder, in view of Svenson in view of Hamasur et al as applied to claims 38-45 above and further in Van Nest et al *(U. S. Patent No. 6,451,325, published September 17, 2992).*

Claims 38-46 are drawn to a method of vaccinating a mammal against mycobacterium having antigenically active carbohydrate moieties (ACM) derived from *Mycobacterium tuberculosis* which comprises mucosal administration to the mammal of

a protection-inducing amount of a tuberculosis vaccine formulation comprising as adjuvant one or more substances and further comprising soybean oil.

The teachings of Schroder, Svenson and Hamasur et al have been discussed above.

Van Nest et al teach the use of any metabolizable oil (for example, soybean oil) in an adjuvant formulation (column 3, lines 62-67 – column 4, lines 1-11). Van Nest et al teach that the oil component of the adjuvant can be present in an amount from 0.5% to 20% by volume (column 4, lines 49-53).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention to add soybean oil as taught by Van Nest to the vaccine formulation a combined above used in the method of vaccinating animals because Schroder teaches that the vaccine composition may contain additional pharmaceutical excipients may be added to the vaccine formation (page 5) and Van Nest et al teach that metabolizable oils such as soybean oil are used in vaccines because unmetabolizable oils when administered may cause abscesses, granulomas or even carcinomas and meat of birds and animals vaccinated with oil other than metabolizable oils may be unacceptable for human consumption due to the deleterious effect that unmetabolizable oils have on the consumer (column 3, lines 62-67 and column 4, lines 1-3).

Status of Claims

9. No claims are allowed.

Conclusion

10. Any inquiry of the general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308–0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Office Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for the Group 1600 is (703) 308-4242.

Any inquiry concerning this communication from the examiner should be directed to Vanessa L. Ford, whose telephone number is (703) 308-4735. The examiner can normally be reached on Monday – Friday from 7:30 AM to 4:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached at (703) 308–3909.

Vanessa L. Ford
Biotechnology Examiner
May 13, 2003

JAMES O. WILSON
SUPERVISORY PATENT EXAMINER
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